# The EDMVS' Draft Work Plan

Presentation to the EDMVS,
August 18-20, 2003

# Purpose of Today's WorkPlan

- Show progress of EDSP
- Provide the status of each assay
- Project what's next

# Tier I Screening Battery

recommended for consideration by EDSTAC

- Steroidogenesis
- Pubertal - female
- Fish Screen

  aka short term fish  reproduction
- Amphibian Metamorphosis
- Estrogen / Androgen receptor binding
- Hershberger
- Uterotrophic

# Alternative Assays

recommended for consideration by EDSTAC

Tier I

- Aromatase
- Pubertal male
- Adult 14 –day intact male

Tier ?

- In Utero through Lactation

# Tier II Assays
## recommended for consideration by EDSTAC

- Mammalian 2-generation
- Avian 2-gen. Reproduction
- Amphibian Development and Repro.
- Invertebrate (Mysid) Lifecycle
- Fish Lifecycle

# Tier I Assays

# Steroidogenesis

| Milestone | Current Status |
|---|---|
| ▪ DRP/Protocol | ✔ June 02 |
|   -cell based (H295R) | Dev by ORD |
| ▪ Prevalidation | |
|   -sectional testes | |
|     optimization | ✔June 03 & Today |
|   -cell based (H295R) | In Lab soon |
|   -multichem & interlab | to lab Sept 03 |
| ▪ Validation | |
|   -inter-lab | to lab June 04 |

Current Status = dates presented to EDMVS &
other information

# Pubertals – m&f

| Milestone | Current Status |
|---|---|
| **DRP equivalent** | ✔ **Dec 01** |
| **Prevalidation** | |
| **-Single Dose Study** | ✔ **Dec 01** |
| **-Multi-chemical & multi-dose Protocols** | ✔ **Dec 01** |
| **-Multi-chemical & multi-dose to EDMVS Dec 03** | **In statistical analysis** |
| **-Restricted Feeding Study** | ✔ **July 02** |
| **Validation (inter-lab)** | **To lab Jan 04** |

# Fish Screen

| Milestones | Current Status |
|---|---|
| ■ DRP/Protocol | ✔ Mar 02 |
| ■ Prevalidation | |
|    - FHM | ✔ Mar 02 |
|    - FHM w/multi-chemicals | In lab ☺ |
|   - Comparative Study Plans: | ✔ Mar 02 |
|   -Results: Comparative Studies | |
|    Vitellogenin Methods, FHM assays | ✔ Today |
| ■ Validation (inter-lab) | depends on OECD |
|    Phase 1A  (OECD) | Today |
|    Phase 1B  (OECD) | Spring 04 |

# Amphibian Metamorphosis

| Milestone | Current Status |
|---|---|
| 🟥 DRP/Protocol | ✔ July 02 |
| 🟥 Pre-validation | |
| prometamorphosis | |
| - optimize protocol | in lab |
| -protocol demonstration | to lab in 04 |
| 🟥 Validation (inter-lab OECD) | TBD |

# ER / AR binding

## ICCVAM

- Scientific Expert Panel's      May 2002
      retrospective validation
- EDMVS briefed by ICCVAM    July 2002
- Expert Panel  Final Report    Sept 2002
- ICCVAM Final Report      May 2003
- EDSP: AR in lab (preval)    **Aug 02 –Sept 03**
- EDSP: ER in lab (valid)    Aug **02 – May 04**

# Aromatase

| Milestones | Current Status |
|---|---|
| ■ **DRP / Protocol** | ✔ **Mar 02** |
| ■ **Prevalidation** | |
| **-placental microsomal assay** | ✔ **June 03 &** |
| **compare bovine, human,** | **Dec 03** |
| **porcine uterine tissue** | |
| **-comparison: microsomal &** | **"** |
| **recombinant, multi chem** | |
| ■ **Validation (inter-lab)** | **to lab Jan 03** |

# In Utero → Lactation

| Milestone | Current Status |
|---|---|
| **DRP** | ✔Dec 02 |
| -Protocol review | ✔Mar 02 |
| **Prevalidation** | |
| -Protocol Demo | Dec 03 |
| -Multi-chem study | TBD |
| **Validation (inter-lab)** | TBD |

# Tier II Assays

# Mammalian 2-generation

|  Milestone | Current Status |
|---|---|
| ▪ Prevalidation | |
| One-gen. Ext. Protocol | ✔ Dec 02 |
| Propylthiouracil Study | ✔ July 02 |
| One-gen Ext. study | ✔ June 03 |
| ▪ Validation (inter-lab) | TBD |

# Avian 2-gen. Reproduction

| Milestone | Current Status |
|---|---|
| ◼ DRP/Protocol | Today |
| ◼ Prevalidation | |
| -Avian Dosing Study Plan | ✔ Mar 02 |
| -Avian Dose Study | in lab |
| to EDMVS in Fall 04 | |
| -Protocol demo | future |
| ◼ Validation (inter-lab OECD) | future |

# Amphibian Dev. & Repro.

| Milestones | Current Status |
|---|---|
| ■ DRP/Protocol | Spring 04 |
| ■ Prevalidation | |
|    -transferable protocol | future |
|    -multi-chem study | future |
| ■ Validation (inter-lab) | future |

# Mysid Lifecycle

| Milestones | Current Status |
|---|---|
| ■ DRP/Protocol | ✔ July 02 |
| ■ Prevalidation | |
|    -transferable protocol | Spring 04 |
|    -multi-chem study | future |
| ■ Validation (inter-lab OECD) | future |

# Fish Lifecycle

| Milestones | Current Status |
|---|---|
| ■ DRP/Protocol | ✔ Dec 02 |
| ■ Prevalidation | |
|    -protocol demo | In Lab |
|    -multi-chem study | future |
| ■ Validation (inter-lab OECD) | future |

# Spring 2004

- Amphibian DRP
- Amphibian Screen transferable protocol
- Fish Screen multi-chemical results
- Fish Screen Phase 1B (OECD)
- Mysid Transferable Protocol